Methods: The search was conducted in Pubmed, Medline, Lilacs, Scielo, ISI web of knowledge, PEDro and the Cochrane Collaboration. We used the keywords: "knee", "balance", "women" and "rehabilitation" in combination with "osteoarthritis". We selected randomized controlled clinical trials published in English, Portuguese and Spanish over the last 10 years. To verify the methodological quality of selected clinical trials, the PEDro Scale was applied.
Results: A total of 20 studies were found in the electronic search. Of these, only 9 met the inclusion criteria and were analyzed in full. Eight of these 9 studies were classified as having high methodological quality on the PEDro Scale. Although the methods and interventions regarding balance varied widely in these studies, most found significant improvement in the balance of women with knee OA.
Conclusion: Since the studies included in this systematic review were of high methodological quality, we can conclude that the therapeutic exercises they used improved the balance of women with knee OA.

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KNEE SYNOVIAL FLUID FROM ACUTELY INJURED PATIENTS CONTAIN PROTEASES THAT CAN DEGRADE AGGRECAN

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Purpose: Aggrecan, the main proteoglycan in cartilage extracellular matrix, is proteolysed in joint injuries and osteoarthritis. During these conditions, aggrecan, which is bound to hyaluronan in cartilage, is attacked by proteases, and it has been suggested that the released aggrecan fragments can be further degraded by proteases in the synovial fluid environment. Our aim was to find out if purified human aggrecan monomers can be degraded by enzymes in synovial fluid (SF) from patients having suffered from knee injuries.
Methods: Human aggrecan monomers were purified, by CsCl density gradient centrifugation collecting the A1D1 fraction, from arthroplasty osteoarthritic knee cartilage. From two knee injured patients, acutely seeking medical care, SF was aspired and stored on ice. Cell-free SF (SF-sup) was prepared by centrifugation at 10 000 xg collecting the supernatant. SF or SF-sup (3, 10 or 30 µl) was added to aggrecan monomers (52 µg dry weight) and incubated in protease digestion buffer (50 mM Tris, 100 mM NaCl, 10 mM $CaCl_2$, pH 7.5) for 24h at 37°C. As an inhibition control TIMP-3 was added at a concentration of 0.65 µM. Aggrecan fragments were then purified either by Alcian blue precipitation or by boiling the samples for 5 min and after centrifugation collecting the aggrecan in the supernatant. The samples were deglycosylated and visualized by Western blot using anti-aggrecan neoepitope antibodies ARGS, FFGV, SELE and an anti-aggrecan G3 antibody.
Results: Incubation for 24h of purified aggrecan monomers in protease digestion buffer without addition of SF did not generate fragmentation of aggrecan (Fig. 1). However, aggrecan incubation with either SF or SF-sup resulted in aggrecan degradation, seen by Western blot as newly formed 140-250 kDa G3 fragments (Fig. 1). SF concentration dependent proteolysis was observed and the generation of G3 fragments was inhibited in the presence of TIMP-3 (Fig. 1). Further analysis showed that the SF and SF-sup induced aggrecanolysis was caused by aggrecanase activity, where the proteases digested aggrecan both in the interglobular domain (IGD), seen as 320 and 120-160 kDa ARGS fragments (Fig. 1), and in the chondroitin sulfate enriched region generating SELE fragments (not shown). SF and SF-sup matrix metalloprotease activity against the aggrecan IGD, generating N-terminal FFGV fragments was also observed. Due to the high protein concentration in SF, to allow detection of aggrecan it was necessary to extract the aggrecan fragments from the sample mixture, and both purification methods (Alcian blue precipitation and boiling) resulted in a similar aggrecan fragment pattern.
Conclusions: Aggrecanolysis was observed after incubation of aggrecan monomers with freshly aspired SF from patients suffering from knee injuries. This suggests that SF from these patients contain active proteases that could degrade aggrecan released from the cartilage. Since also cell-free SF was able to cleave aggrecan, this further suggests that the proteases were already extracellular at the time of SF aspiration.

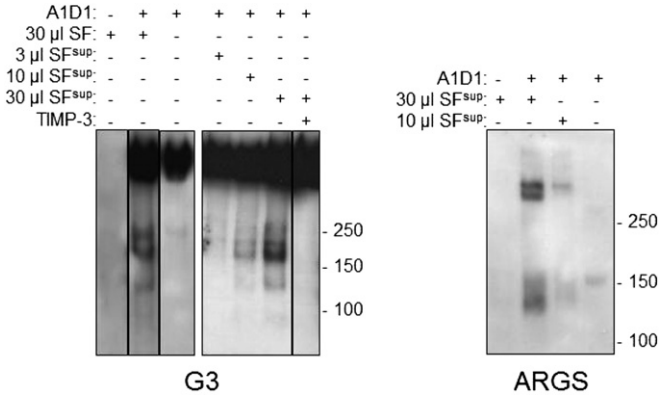

Figure 1. Aggrecan (A1D1) was incubated for 24h in the presence or absence of SF or cellfree SF (SF^{sup}). Aggrecan was then purified and run on Western blot using G3 and ARGS antibodies.

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MECHANOBIOLOGICAL RESPONSE OF CHONDROCYTES TO A TMJ-SPECIFIC LOADING PATTERN OVER TIME

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Purpose: Remodeling of cartilage is a physiological response to mechanical loading. Persistent mechanical overloading, however, induces irreversible mechanical and biological changes within the tissue, thus quickening the potential development of degenerative joint disease. Yet, the exact mechanobiological processes prompting chondrocytes to induce catabolism remain widely unknown. Combined anatomical and kinematic in vivo data of human TMJs give insight into strains, stresses and forces within asymptomatic and diseased joints during loading and reveal complex rolling/plowing patterns acting on the articular disc. The transfer of this knowledge into a biological model helps to gain more understanding of the cellular and biochemical processes leading to cartilage failure und ultimately osteoarthritis.
Methods: With a previously developed rolling/plowing explant test system, mechanical load was applied to cartilage explants (from bovine nasal septum) for 2 hours. Cartilage specimens ($2 \times 17 \times 70$ mm) were exposed to combined compression and translation of a cylindrical indenter at 100 N and 10 mm/s, respectively. Control samples ($2 \times 12 \times$ 70mm) were kept in unloaded culture under the same conditions. Gene regulation of extracellular matrix (ECM) proteins (collagen 1 and 2, aggrecan and fibronectin), ECM enzymes (matrix metalloproteinase 3 (MMP3), tissue inhibitor of metalloproteinase 1(TIMP1)) and lubricin were investigated with quantitative real-time polymerase chain reaction (qRT-PCR). Water gain/loss of each sample was examined immediately after plowing and again at 2, 4, 8 and 24 hours post-loading. In addition, the development of shear forces over the plowing period was recorded.
Results: qRT-PCR showed that MMP3 was upregulated (2.2×) at 2 and 4 hours after loading and continued to stay upregulated until 8 hours postloading (3.2×) whereas TIMP1 tended to decrease over time. Lubricin expression showed a 2.4× and 5.6× upregulation after 4 and 8 hours, respectively. Genes for matrix proteins did not seem to be upregulated within 24 hours post-loading with our loading parameters. Yet, collagen 2, aggrecan and fibronectin showed a trend towards higher expression after 4 and up to 24 hours. The mechanical data of the loading device clearly showed an increase of shear forces over the 2 hour plowing period. Cartilage samples mostly seemed to incorporate water into the ECM 8 hours post-loading.
Conclusions: This study indicates that a possible ECM remodeling process following a 2-hour plowing treatment starts 4 hours post-loading with the increase of MMP3, collagen 2 and aggrecan expression. This is supported by the fact that swelling-induced weight gain starts after 8 hours, indicating the breakdown of the collagen structures and that most of biological response occurs after 4 hours post-loading. Lubricin upregulation indicates an attempt of chondrocytes to counteract increasing shear stresses acting on the surface with ongoing plowing. Further experiments with a longer sampling period are needed to investigate a possible late response of matrix protein expression.